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CHARACTERISTICS OF VASCULAR PERMEABILITY  
IN EXPERIMENTAL HYPERTENSION

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# CHARACTERISTICS OF VASCULAR PERMEABILITY IN EXPERIMENTAL HYPERTENSION.

-USSR-

Following is the translation of an article entitled "K Kharakteristike Sosudnoi Pronitsaemosti Pri Eksperimentalnoi Gipertonii" (English version above) by M.F. Sirotina in Patologicheskaya Fiziologia i Eksperimental'naya Terapiya (Pathological Physiology and Experimental Therapy), Vol IV, No. 4, Moscow 1960, pages 39-41.

Changes in the vascular system during hypertonic ailments are complex and insufficiently studied.

In the initial stages of the development of hypertension, functional impairment of the vascular system is observed (7). Later, these impairments are complicated by morphological changes (1,4,5,12,14). It is well known that one of the symptoms of functional and morphological disorders of the vascular system during hypertension is the impairment of peripheral circulation.

A number of research workers studying the state of blood vessel walls in hypertension found an increased permeability of the walls (6,8,9,13,15). Others come to the opposite conclusions (3,11,14).

One must suppose that this disagreement arises in large part from the particular experimental methods used by the research workers. We studied vascular permeability in male rabbits; first in normal animals, then at various stages after renal hypertension had been induced in them.

We conducted this study of vascular permeability with the aid of albumin tagged with the isotope  $J^{131}$ , since it is known that the determination of the rate of exit of large molecule complexes from the vascular channels is the best way of studying the changes in the whole system of capillary permeability. This is especially true of albumin.

The possibility of using tracer proteins marked with radioactive isotopes has opened wide opportunities for the objective study of the functional state of the vascular system.

We extracted methylalbumin from ox blood by salting out with ammonium sulphate. The  $J^{131}$  we derived by the method used in the laboratory of I.A. Oivin. The basic iodizing method of Francis, Mulligan and Wormel was applied.

The tagged albumin was introduced into the marginal vein of the rabbit's ear in concentrations of two to four milligrams/kilogram, depending on the degree of its radioactivity. Blood was taken from the other ear after intervals of five, thirty, sixty, ninety and one hundred and twenty minutes. The radioactivity count was made with 0.1 ml. of blood with the use of a scintillometer. We generally took two simultaneous tests. The radioactivity of the blood after five minutes was equated to 100%. The number of impulses was counted during a five minute period. From data thus derived, we subtracted the background amount.

During the study of vascular permeability in the case of albumin, it was interesting to note the changes in the formed elements and in the composition of blood albumin. We conducted the study of the composition of blood albumin by the salting-out diffusion process worked out by N.V. Zelenski at the Physiological Institute of A.A. Bogomoletz, Academy of Sciences, Ukrainian Soviet Socialist Republic. The full albumin composition in the blood was determined, including the albumin composition of the plasma and the simultaneously formed blood elements. In this particular work we make use of only certain indices, viz. 1. the sum total of albumins (plasma albumins plus the albumins of formed elements); 2. the quantity of plasmas fibrinogens; 3. quantity of albumins, globulins, serum, and the albuminglobulin ratio (A/G). The figures are expressed in grams per cent on the basis of whole blood.

Animals thus observed had their carotid artery brought out into a skin flap in order to measure the blood pressure by the bloodless method. Perforated silver rings were then applied to the renal artery; that is, we induced, experimentally, a renal hypertension using Gorev's method.

The experiments were conducted with sixteen rabbits. Five animals were re-examined three to four months after the inception of induced hypertension. Eleven were re-examined after six months.

The arterial pressure of animals with hypertension went up by 40-55 mm.

Both groups of rabbits showed a marked increase in vascular permeability. When the data were subjected to the

methods of statistical variation, the results substantiated the arithmetical average. In the normal rabbits of the first group, the radioactivity of the blood decreased by 15%, on the average, thirty minutes after introduction of J131. After sixty minutes, it decreased by 30%; after 90 minutes -- by 36%; after 120 minutes -- by 44%. In rabbits with hypertension, the corresponding percentages were 27%, 35%, 46% and 56%. This means that the rate of albumin J131 removal from the blood increased after development of hypertension in the rabbits of this group (fig 1).

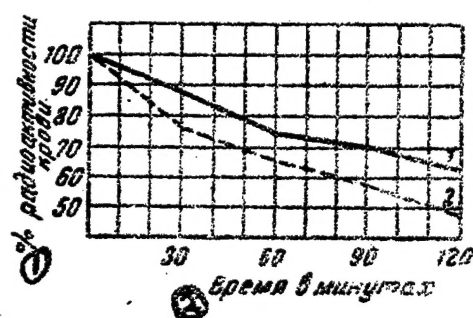


Fig 1. Rate of passage of tagged J131 from blood in normal rabbits with experimentally induced hypertension (3 months after onset of hypertension). 1) percent of radioactivity in blood; 2) time in minutes

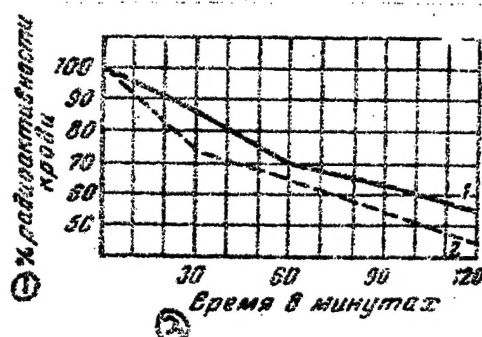


Fig 2. Rate of passage of tagged J131 from blood of normal rabbits and from blood of rabbits with experimentally induced hypertension (6 months after onset of hypertension).

In normal rabbits of the second group, the radioactivity of the blood decreased, on the average, by 12% thirty minutes after introduction of J131. After sixty minutes it decreased by 26%; after 90 minutes -- by 30%; after 120 minutes -- by 37%. After development of hypertension in these same animals, the corresponding decreases in radioactivity were 24%, 35%, 42%, and 52%. In this group, as in the first, vascular permeability increased (fig 2).

Vascular permeability showed no significant changes in normal animals during the three month period.

Albumin concentration in the blood of the experimental rabbits was raised (in six out of nine examinations) in comparison with the initial, pre-experimental stage.

The amount of fibrinogen in the plasma increased appreciably in almost every case. The quantity changes in serum globulins did not follow a pattern, but the albumin level of the serum tended to decrease. The A/G ratio decreased in six cases (Table 1).

Table 1.

① Изменение белкового состава крови у кроликов при экспериментальной гипертонии (в г%)

⑦ № кролика	③ Нормальные кролики					① Кролики с гипертонией				
	④ общий белок	⑤ фибриноген плазмы	⑥ глобулины сыворотки	⑦ альбумины сыворотки	⑧ А/Г коэф-фици-ент	④ общий белок	⑤ фибриноген плазмы	⑥ глобулины сыворотки	⑦ альбумины сыворотки	⑧ А/Г коэф-фици-ент
1	17,80	0,20	1,20	1,20	1,0	20,58	0,24	1,12	1,22	1,1
2	21,94	0,20	0,10	1,64	1,4	23,00	0,46	1,24	1,50	1,2
3	19,82	0,20	1,16	1,46	1,2	18,76	0,34	1,04	1,00	1,0
4	19,94	0,16	0,90	1,54	1,3	21,30	0,30	1,26	1,32	1,0
5	21,66	0,24	0,92	1,50	1,6	22,80	0,32	1,18	1,70	1,4
6	15,80	0,23	1,12	1,45	1,3	25,90	0,58	1,14	1,98	1,7
7	22,16	0,29	1,51	1,66	1,1	19,84	0,44	1,19	1,61	1,3
8	15,60	0,24	0,9	1,16	1,3	20,00	0,38	0,86	1,36	1,5
9	19,78	0,24	0,86	1,38	1,5	18,98	0,30	1,00	1,28	1,3

1) Changes in albumin composition in blood of rabbits with experimentally induced hypertension 2) No. of rabbit 3) normal rabbits 4) general albumin 5) plasma fibrinogen 6) serum globulins 7) serum albumins 8) A/G coefficient 9) hypertonic rabbits

The hemoglobin level increased or remained unchanged in rabbits with hypertension (hypertension of six months' duration). In most cases, the erythrocyte count increased, while the leucocyte count tended to decrease in hypertension of indicated duration (Table 2).

Table 2.

① Изменение гемоглобина, эритроцитов и лейкоцитов крови при экспериментальной гипертонии

② № кролика	③ Кролики нормальные			① Кролики с гипертонией		
	④ Hb (в %)	⑤ эр. (млн/мм³)	⑥ л. (г/мм³)	④ Hb (в %)	⑤ эр. (млн/мм³)	⑥ л. (в мм³)
1	104	6,5	4 800	114	8,0	5 300
2	90	5,8	7 800	104	7,5	7 400
3	90	5,6	8 100	90	5,8	7 300
4	100	6,5	6 800	100	7,7	7 300
5	95	6,7	6 600	94	7,1	12 600
6	84	5,0	8 400	94	6,5	7 000
7	95	7,0	7 500	87	5,9	5 000
8	87	7,0	7 500	86	7,0	6 700
9	90	5,4	8 700	90	6,0	6 300

Legend to Table 2: A) Normal rabbits B) No. of rabbit  
C) hemoglobin (%) D) erythrocyte count (million/cu mm)  
E) leucocytes (in mm<sup>3</sup>) F) rabbits with hypertension

### CONCLUSIONS

1. In experimentally induced renal hypertension in rabbits, the use of albumin tagged with J131 showed an increase in vascular permeability.

2. In experimentally induced hypertension, the albumin composition changes in the peripheral blood. The albumin concentration in the blood and the fibrinogen in the plasma increase. The albumin concentration in the serum tends to decrease, as well as the A/G ratio.

When hypertension has become established, the erythrocyte count increases, while the leucocyte count tends to decrease per unit volume of blood.

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